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PATENT & TRADEMARK OFFICE

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Francis J. GILES et al. Examiner: Cybille Delacroix-Muirheid

Serial No.: 10/729,387 Group Art Unit: 1614

Filed: December 8, 2003

For: PHARMACEUTICAL COMBINATIONS AND METHODS FOR THE TREATMENT OF LEUKEMIA

REPLY BRIEF PURSUANT TO 37 C.F.R. §41.41

MAIL STOP: APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Examiner's Answer issued October 2, 2008, Appellants' submit the following Reply Brief, pursuant to 37 CFR §41.41). While it is believed that there are no fees for filing this Reply Brief, the Commissioner is hereby authorized to charge any fees associated with this Reply Brief or credit any overpayment to Deposit Account No. 13-3402.

1. Structurally Divergent Compounds

At page 11 of the Examiner's Answer, it is argued that it would be reasonable for one skilled in the art to expect that synergism would occur between STI-571 and (-)-L-OddC (aka (-)-β-L-Dioxolane-Cytidine) since synergism was found for STI-571 and four structurally divergent compounds. Appellants disagree.

From an asserted synergism with four compounds, it would not be reasonable for one skilled in the art reasonable to extrapolate an expectation that STI-571 will exhibit synergism with **any other anti-leukemia agent regardless of the structure of that agent**. The structure of the compounds will clearly affect the pharmacology and pharmacokinetic

behavior of a compound, and compounds that are structurally divergent will be expected to exhibit different pharmacology and pharmacokinetic behavior.

For example, one skilled in the art could not reasonably expect that a compound having a structure divergent from the four prior art agents would not adversely interact with STI-571. Nor could one skilled in the art reasonably expect that the activity of a compound having a structure divergent from the four prior art agents would be enhanced by the presence of STI-571, as clearly the mechanisms of interaction, due to differences in structure, would be different than those in which synergy was reported.

2. Inhibition of Bcr-Abl tyrosine kinase

At page 11 of the Examiner's Answer, it is asserted that the mechanism of action of STI-571, asserted to be the inhibition of Bcr-Abl tyrosine kinase, does not change when administered with compounds having different structures. This broad conclusion is not supported by the results of only four compounds. Other structurally different compounds may readily interfere with the inhibition of Bcr-Abl tyrosine kinase. Furthermore, the Examiner's Answer fails to demonstrate that inhibition of Bcr-Abl tyrosine kinase will necessarily result in synergism between STI-571 and all anti-leukemia agents, regardless of their structure and mechanism of action. Unless there is a reasonable expectation that inhibition of Bcr-Abl tyrosine kinase will enhance the activity of all ant-leukemia agents, there can be no reasonable expectation that synergism will occur between STI-571 and other anti-leukemia agents.

3. Commensurate in Scope

In the paragraph bridging pages 11-12 of the Examiner's Answer, the Examiner argues that the data presented in appellants' specification is not commensurate in scope. This argument appears to contradict the Examiner's prior argument. On the one hand, the Examiner argues that it is a reasonable extrapolation that compounds will exhibit synergism with STI-571 based on an asserted showing of synergism between STI-571 and four **structurally divergent** compounds. On the other hand, the Examiner argues that it would not be reasonable to extrapolate that compounds (i.e., other compounds of appellants' formula I) will exhibit synergism with STI-571 based on an asserted showing of synergism

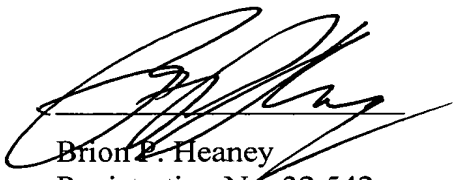
between STI-571 and a structurally similar compound (i.e., (-)-L-OddC).

The compounds of appellants' formula I are clearly structurally similar. It is not unreasonable to extrapolate results of synergy shown for one compound of a relatively small genus to other members of that genus. Furthermore, the method claims specify that amounts administered are effective and both composition and method claims specify a ratio of the active agents. In addition, many of appellants' claims recite specific stereochemistry of the compound of Formula I. See, e.g., claims 7, 9, 10, 22, 31, 32, and 52-62.

For these reasons, contrary to the assertion in the Examiner's Answer, appellants' data are commensurate with the scope of the claimed invention.

For all of the above reasons, and those presented in appellants' Appeal Brief, it is again urged that the decision of the Examiner finally rejecting claims 1, 7, 9, 10, 14, 15, 17-22, 25-32, 39-45, and 52-64, on appeal, is in error and should be reversed.

Respectfully submitted,



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